Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A modified cytoplasmic dynein heavy chain1 polypeptide, wherein:

(a) the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of at least one amino acid in the wild type cytoplasmic dynein heavy chain1 sequence;

(b) a biological activity of said modified cytoplasmic dynein heavy chain1 polypeptide is altered by at least 10% in comparison to the activity of the wild type cytoplasmic dynein heavy chain1 polypeptide.

2. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 1, wherein said biological activity is altered by at least 50% or by at least 75% in comparison to the activity of the wild type cytoplasmic dynein heavy chain1 polypeptide.

3. (Canceled)

4. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 1, wherein the alteration of said biological activity is any one of a reduction or an increase of activity.

5. (Canceled)

6. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 1, wherein the alteration of said biological activity is demonstrated by a method selected from the group consisting of:

(a) determining the relative proportions of cytoplasmic dynein heavy chain1 dimer and cytoplasmic dynein heavy chain1 monomer in a test sample;

(b) quantifying the proportion of cytoplasmic dynein complex that is fully assembled from its subunits in an *in vitro* assembly assay;

(c) quantifying the proportion of cytoplasmic dynein complex subunits that remain unassembled in an *in vitro* assembly assay;

(d) quantifying the proportion of cytoplasmic dynein heavy chain1 that binds to microtubules *in vitro*;

(e) assaying the rate of dimerization of the cytoplasmic dynein heavy chain1 polypeptide *in vitro*;

(f) assaying the rate of assembly of the cytoplasmic dynein complex from constituent subunits *in vitro*;

(g) assaying the rate of binding of cytoplasmic dynein heavy chain1 to microtubules *in vitro*;

(h) assaying motor activity of the cytoplasmic dynein complex *in vitro*; and

(i) assaying motor activity of the cytoplasmic dynein heavy chain1 *in vitro*; and

wherein the method compares the results provided by said modified cytoplasmic dynein heavy chain1 polypeptide to those provided by the corresponding wild type cytoplasmic dynein heavy chain1 polypeptide.

7. (Canceled)

8. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 1, wherein the alteration of said biological activity is demonstrated by assaying motor activity of the cytoplasmic dynein heavy chain1 *in vitro*, wherein motor activity of the cytoplasmic dynein heavy chain1 is determined *in vitro* by at least one parameter selected from the group consisting of:

(a) rate of total protein transport through cellular Golgi apparatus;

(b) axonal transport;

(c) retrograde axonal transport;

(d) microtubule gliding rate;

(e) phagosome movement along microtubules;

(f) rate of intracellular trafficking of membranous organelles;

(g) nuclear migration rate; and

(h) prometaphase chromosome movement.

9. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide according to claim1, wherein expression of the protein within a non-human animal model heterozygous for the modified and wild type cytoplasmic dynein heavy chain1 gene results in the animal developing at least one of the following phenotypical features:

(a) epilepsy;

(b) myoclonic cramping;

(c) neuronal excitotoxicity;

(d) cell damage in hippocampus;

(e) cell damage in cerebellum;

(f) neurodegenerative disease;

(g) under-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(h) under-expression, under-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(i) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1.

10. (Original) The modified cytoplasmic dynein heavy chain1 polypeptide according to claim 9 wherein the phenotypical features developed by said non-human animal model comprise at least one feature selected from the following group:

(a) myoclonic cramping of the fore limbs;

(b) myoclonic cramping of the hind limbs;

(c) cell damage in CA3 and CA4 sectors of hippocampus;

(d) cell damage in gyrus dentatus;

(e) neuronal damage in the upper layer of the cortex and in the Purkinje cell layer of the cerebellum;

(f) motor neuron impairment;

(g) Alzheimer's disease;

(h) Parkinson's disease;

(i) amyotropic lateral sclerosis;

(j) spinal muscular atrophy; and

(k) fiber type grouping in *Musculus tibialis anterior*.

11. (Previously Presented) A modified cytoplasmic dynein heavy chain1 polypeptide, wherein:

(a) the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of at least one amino acid residue in the wild type cytoplasmic dynein heavy chain1 sequence;

(b) the position of said amino acid residue in the cytoplasmic dynein heavy chain1 sequence is selected from:

those positions at which, in each of the wild type cytoplasmic dynein heavy chain1 reference sequences, the identity of the wild type amino acid residue is conserved; and

(c) said wild type cytoplasmic dynein heavy chain1 reference sequences consist of:

(i) SEQ ID NO:18 (*Homo sapiens*);

(ii) Genbank Accession No. NP_062099 (*Rattus norvegicus*); and

(iii) Genbank Accession No. NP_084514 (*Mus musculus*).

12 -13. (Canceled)

14. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 11, wherein said amino acid residue corresponds to a residue selected from the group of conserved amino acid residues between Leu302 (302L) and Phe1140 (1140F) of SEQ ID NO:2 (*Mus musculus*) specified in Table 19.

15. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 11, wherein said amino acid residue is positioned in a cytoplasmic dynein heavy chain1 domain capable of binding a subunit of the cytoplasmic dynein complex selected from the group consisting of:

(a) cytoplasmic dynein heavy chain1;

(b) cytoplasmic dynein intermediate chain; and

(c) cytoplasmic dynein light intermediate chain.

16. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 11, wherein said amino acid residue is positioned in the cytoplasmic dynein heavy chain1 dimerization binding domain.

17. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 11, wherein said amino acid residue is located in a sequence selected from the group consisting of:

(a) sequences encoded by cytoplasmic dynein heavy chain1 exon 13;

(b) SEQ ID NO:21;

(c) SEQ ID NO:23;

(d) sequences encoded by cytoplasmic dynein heavy chain1 exons 12 and 13;

(e) SEQ ID NO:22; and

(f) SEQ ID NO:24.

18. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 11, wherein said amino acid residue is located in a position corresponding to a residue selected from the group consisting of:

(a) in SEQ ID NO:2 (*Mus musculus*),

(i) residue 300 to residue 1140;

(ii) residue 416 to residue 701;

(iii) residue 649 to residue 800;

(b) in SEQ ID NO:18 (*Homo sapiens*); and

(i) residue 302 to residue 1142;

(ii) residue 418 to residue 703;

(iii) residue 651 to residue 802.

19. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 18 wherein said amino acid residue is located in a position corresponding to a residue selected from the group consisting of:

(a) in SEQ ID NO:2 (*Mus musculus*), residue 649 to residue 701; and

(b) in SEQ ID NO:18 (*Homo sapiens*), residue 651 to residue 703.

20. (Canceled)

21. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 11, wherein the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of at least ten of said amino acid residues.

22. (Canceled)

23. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 11, wherein said amino acid residue is selected from the following group:

(a) a residue at a position within ten residues of position 1055 of the amino acid sequence as shown in SEQ ID NO:2;

(b) a residue at a position within ten residues of position 1057 of the amino acid sequence as shown in SEQ ID NO:18; and

(c) a residue corresponding to one of the residues of the amino acid sequence VEQYVKVWLQYQCLWDMQAEN (SEQ ID NO:113).

24 – 26. (Canceled)

27. (Previously Presented) A modified cytoplasmic dynein heavy chain1 polypeptide, wherein the modification is an amino acid substitution in the wild type cytoplasmic dynein heavy chain1 sequence at a position selected from the group consisting of:

(a) a position corresponding to position 1055 of the amino acid sequence as shown in SEQ ID NO:2; and

(b) a position corresponding to position 1057 of the amino acid sequence as shown in SEQ ID NO:19.

28. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide according to claim 1, wherein the modified cytoplasmic dynein heavy chain1 polypeptide is a mammalian cytoplasmic dynein heavy chain1 polypeptide selected from the group consisting of:

(a) human cytoplasmic dynein heavy chain1 polypeptide;

(b) murine cytoplasmic dynein heavy chain1 polypeptide; and

(c) rat cytoplasmic dynein heavy chain1 polypeptide.

29 -30. (Canceled)

31. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 1, wherein said substitution, deletion, or insertion of at least one amino acid residue in the wild type cytoplasmic dynein heavy chain1 sequence is located within a region of the polypeptide selected from the group consisting of:

(a) the region encoded by exon 12;

(b) the region encoded by exon 13;

(c) the cytoplasmic dynein heavy chain1 dimerization domain; and

(d) a cytoplasmic dynein heavy chain1 binding domain for a subunit of the cytoplasmic dynein complex distinct from cytoplasmic dynein heavy chain1.

32. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide of claim 1, wherein said deletion is of more than one amino acid residue in the wild type cytoplasmic dynein heavy chain1 sequence and extends into a region of the polypeptide selected from the group consisting of:

(a) exon 12;

(b) exon 13;

(c) the cytoplasmic dynein heavy chain1 dimerization domain; and

(d) a cytoplasmic dynein heavy chain1 binding domain for a subunit of the cytoplasmic dynein complex distinct from cytoplasmic dynein heavy chain1.

33. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide according to claim, wherein the amino acid substitution replaces a Tyr residue.

34. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide according to claim 1, wherein said amino acid substitution is with an amino acid residue selected from the group consisting of Met, Leu, Ile, Val and Cys.

35. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide according to claim 34, wherein the amino acid substitution is with a Cys residue.

36. (Previously Presented) The modified cytoplasmic dynein heavy chain1 polypeptide according to claim 35, wherein the modified cytoplasmic dynein heavy chain1 polypeptide has an amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:6.

37. (Previously Presented) A cytoplasmic dynein heavy chain1 polypeptide comprising the polypeptide according to claim 1.

38. (Original) A murine cytoplasmic dynein heavy chain1 polypeptide having an amino acid sequence of SEQ ID NO:4.

39. (Original) A human cytoplasmic dynein heavy chain1 polypeptide having an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:6; and

(b) the amino acid sequence as shown in SEQ ID NO:18.

40 – 43. (Canceled)

44. (Previously Presented) A composition comprising:

(a) a polypeptide selected from the group consisting of:

(i) the cytoplasmic dynein heavy chain1 polypeptide of claim 1;

(ii) the in-frame amino acid sequence derived from exon 12 of Dchc;

(iii) the in-frame amino acid sequence derived from exon 13 of Dchc; and

(iv) the in-frame amino acid sequence derived from exons 12 and 13 of Dchc; and

(b) a pharmaceutically acceptable carrier.

45. (Canceled)

46. (Previously Presented) A polynucleotide, preferably isolated, comprising a nucleic acid sequence encoding a cytoplasmic dynein heavy chain1 polypeptide of claim 1.

47 – 48. (Canceled)

49. (Previously Presented) A polynucleotide, preferably isolated, comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the following group:

(a) SEQ ID NO: 18;

(b) SEQ ID NO: 21;

(c) SEQ ID NO: 22;

(d) SEQ ID NO: 23; and

(e) SEQ ID NO:24.

50 – 78. (Canceled)

79. (Previously Presented) A method for the prevention, treatment or amelioration of a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject, particularly a human subject, comprising the step of administering to the subject a cytoplasmic dynein heavy chain1 polypeptide of claim 1.

80. (Canceled)

81. (Previously Presented) A method of preventing, treating or ameliorating a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject, particularly a human subject, comprising the step of administering to the subject the composition of claim 44.

82. (Previously Presented) A method of diagnosing in a mammalian subject, particularly a human subject, at least one of:

(a) a cytoplasmic dynein heavy chain1-mediated medical condition;

(b) a susceptibility to develop a cytoplasmic dynein heavy chain1-mediated medical condition;

wherein the method comprises the steps of:

(i) isolating a biological sample from the subject;

(ii) comparing expression levels of cytoplasmic dynein heavy chain1 in the subject sample against a reference value, wherein said reference value is obtained by performing the method with a wild type sample equivalent to the biological sample from the subject, wherein a positive diagnosis is indicated by determining a cytoplasmic dynein heavy chain1 expression level in the subject sample that differs from that in the wild type sample by a factor selected from the group consisting of:

(a) expression in subject sample being less than 50% of expression in wild type sample;

(b) expression in subject sample being less than 20% of expression in wild type sample;

(c) expression in subject sample being less than 5% of expression in wild type sample;

and wherein the expression level of cytoplasmic dynein heavy chain1 in the subject sample is at least 0.5% of that in the wild type sample.

83 – 84. (Canceled)

85. (Previously Presented) The method of claim 82, wherein said expression level of cytoplasmic dynein heavy chain1 is determined by detecting the existence of a mutation in a nucleic acid sequence controlling the level of expression of the cytoplasmic dynein heavy chain1 polypeptide.

86. (Previously Presented) A method of diagnosing in a mammalian subject, particularly a human subject, at least one of:

(a) a cytoplasmic dynein heavy chain1-mediated medical condition;

(b) a susceptibility to develop a cytoplasmic dynein heavy chain1-mediated medical condition;

wherein the method comprises the steps of:

(i) isolating a sample of nucleic acid from the subject; and

(ii) determining that said sample comprises a mutation in the nucleic acid sequence of a polynucleotide encoding the cytoplasmic dynein heavy chain1 polypeptide, wherein said mutation is responsible for a substitution, deletion or insertion of at least one amino acid residue in the encoded polypeptide.

87. (Previously Presented) The method of claim 86, wherein said method comprises the additional step of identifying said mutation.

88. (Canceled)

89. (Previously Presented) The method of claim 86, wherein the method comprises the additional step of determining that the cytoplasmic dynein heavy chain1 encoded by said polynucleotide is a modified cytoplasmic dynein heavy chain1 polypeptide of claim 1.

90 – 91. (Canceled)

92. (Previously Presented). The method of claim 86, wherein said method comprises the additional step of confirming that said mutation is associated with at least one of:

(a) a cytoplasmic dynein heavy chain1-mediated medical condition;

(b) a susceptibility to develop a cytoplasmic dynein heavy chain1-mediated medical condition;

wherein said confirmation is obtained by an analysis selected from the group consisting of:

(i) a structural analysis of cytoplasmic dynein heavy chain1 comprising said mutation;

(ii) assaying a biological function of cytoplasmic dynein heavy chain1 comprising said mutation,

wherein said analysis comprises at least one method selected from the group consisting of:

(a) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation is capable of dimerization;

(b) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation binds a recombinantly produced peptide corresponding to the dimerization domain of cytoplasmic dynein heavy chain1, preferably corresponding to the dimerization domain of human cytoplasmic dynein heavy chain1;

(c) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation binds other components of the dynein complex selected from the group comprising:

(i) dynein intermediate chain;

(ii) dynein light intermediate chain;

(iii) dynein light chain;

(iv) dynactin;

(v) dynamitin;

(d) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation is capable of integration into an intact dynein complex;

(e) assaying whether formation of intact dynein complex is inhibited in the presence of the cytoplasmic dynein heavy chain1 comprising said mutation;

(f) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation is capable of actin movement; and

(g) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation is capable of axonal transport.

93 – 95. (Canceled)

96. (Previously Presented) The method of claim 86, wherein the mutation is located in the nucleic acid sequence encoding cytoplasmic dynein heavy chain1, wherein cytoplasmic dynein heavy chain1 is selected from SEQ ID NO:17.

97. (Previously Presented) The method of claim 86, wherein the mutation is located in a selected region of the nucleic acid sequence encoding cytoplasmic dynein heavy chain1, wherein said selected region is selected from the group consisting of:

(a) exon 12;

(b) exon 12 and exon 13; and

(c) the dimerization binding site of cytoplasmic dynein heavy chain1.

98. (Previously Presented) The method of claim 97, wherein the mutation is located in cytoplasmic dynein heavy chain1, wherein said selected region comprises the amino acid sequences, selected from the group consisting of:

(a) SEQ ID NO:23;

(b) SEQ ID NO:24; and

(c) residues 302 to residues 1142 in SEQ ID NO:18.

99. (Previously Presented) The method of claim 86, wherein said medical condition is a neurodegenerative disease.

100. (Previously Presented) The method of claim 99, wherein said neurodegenerative disease is a progressive neurodegenerative disease and is selected from the group of Alzheimer's disease, Parkinson's disease, amyotropic lateral sclerosis and spinal muscular atrophy.

101 – 121. (Canceled)

122. (Original) A method of identifying a protein or nucleic acid marker indicative of an increased risk of a mammalian subject, particularly a human subject, of developing a neurodegenerative disease, said method comprising the step of analyzing a test sample derived from said subject for the presence of a difference compared to a similar test sample if derived from a subject of the same species unaffected by or known not to be at risk of developing said disease, wherein said difference is indicative of the presence of a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex.

123. (Original) A method of identifying a protein or nucleic acid marker indicative of an association of a neurodegenerative disease in a mammalian subject, particularly a human subject, with a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex, said method comprising the step of analyzing a test sample derived from said subject for the presence of a difference compared to a similar test sample if derived from a subject of the same species, unaffected by or known not to be at risk of developing said disease, wherein said difference is indicative of the presence of a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex.

124. (Previously Presented) The method of claim 122, wherein said test sample is analyzed for a difference compared to similar test samples if derived from a group of mammalian subjects of the same species as said subject, which subjects are unaffected by, or known not to be at risk of developing, said neurodegenerative disease.

125. (Previously Presented) The method according to claim 122, wherein said mammalian subject whose test sample is analyzed has a neurodegenerative disease or is known or suspected to be at risk of developing a neurodegenerative disease.

126 – 151. (Canceled)

152. (Original) A method for identifying a predisposition of a mammalian subject, particularly a human subject, for developing a neurodegenerative disease, said method comprising the step of determining whether a test sample derived from said subject indicates the presence of a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex, indicative of an increased risk of said subject of developing said neurodegenerative disease.

153. (Canceled)

154. (Original) A method for determining whether a neurodegenerative disease in a mammalian subject, particularly a human subject, is associated with a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dyncin complex, said method comprising the step of determining whether a test sample derived from said subject indicates the presence of a mutation in an allele of a gene coding for said protein.

155. (Previously Presented) The method according to claim 152, wherein said neurodegenerative disease is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, and Huntington's Disease.

156. (Previously Presented) The method according to claim 152, wherein said neurodegenerative disease is a motorneuron degenerative disease.

157. (Original) The method according to claim 156, wherein said motorneuron degenerative disease is selected from the group consisting of: Amyotrophic Lateral Sclerosis, Spinal Muscular Atrophy, Bulbo-Spinal Muscular Atrophy, Progressive Bulbar Palsy, Progressive Muscular Atrophy, and Primary Lateral Sclerosis.

158. (Previously Presented) The method according to claim 152, wherein said test sample is a nucleic acid sample, selected from the group consisting of mRNA, cDNA, and genomic DNA.

159. (Canceled)

160. (Canceled)

161. (Previously Presented) The method according to claim 152, wherein said test sample is a protein sample.

162. (Canceled)

163. (Previously Presented) The method according to claim 152, wherein said mutation selectively affects cell types associated with or suspected to be involved in developing a neurodegenerative disease.

164. (Previously Presented) The method according to claim 152, wherein said mutation selectively affects motorneurons, preferably a-motorneurons.

165. (Previously Presented) The method according to claim 152, wherein said mutation affects a cellular process selected from the group of processes consisting of neuronal axonal transport, cellular transport, proliferation, differentiation and apoptosis.

166. (Previously Presented) The method according to claim 152, wherein said mutation leads to a disruption of, or alteration in the functional interaction within the dynactin/dynein complex in neurons, preferably in motorneurons.

167. (Previously Presented) The method according to claim 152, wherein said mutation results in a deletion or substitution by another amino acid of an amino acid encoded

by said allele, or an insertion of additional amino acids not normally present in the amino acid sequence of said protein, encoded by said allele.

168. (Original) The method according to claim 167, wherein said deletion, substitution, or insertion is encoded by both alleles of the gene coding for said protein.

169. (Previously Presented) The method according to claim 167, wherein said deletion, substitution, or insertion occurs in an evolutionary conserved region of said protein.

170. (Previously Presented) The method according to claim 152, wherein said mutation results in the substitution of an amino acid which is identical between the corresponding mouse and human protein, preferably between the corresponding mouse, rat, and human protein encoded by said allele, by another amino acid.

171. (Previously Presented) The method according to claim 167, wherein said amino acid is substituted by a naturally occurring amino acid.

172. (Previously Presented) The method according to claim 167, wherein said amino acid is encoded by a codon within the open reading frame of a nucleic acid sequence selected from the group consisting of SEQ ID NO.:28-59 or SEQ ID NO.: 70-112 or SEQ ID NO.:114-126.

173. (Previously Presented) The method according to claim 167, wherein said amino acid is located in a domain of said protein, which is capable of binding to another subunit of the dynactin/dynein complex.

174. (Original) The method according to claim 173, wherein said domain is defined by an amino acid sequence selected from the group of sequences consisting of

in case the protein is mouse cytoplasmic dynein intermediate chain 1 (SEQ ID NO.: 61):

i) amino acids 147-157;

ii) amino acid 243-314;

iii) amino acids 140-157; and

iv) amino acids 1-123;

in case the protein is human cytoplasmic dynein intermediate chain 1 (SEQ ID NO.: 62):

v) amino acids 164-174;

vi) amino acids 260-331;

vii) amino acids 157-174; and

viii) amino acids 1-140;

in case the protein is mouse cytoplasmic dynein intermediate chain 2 (SEQ ID NO.: 64):

i) amino acids 1-123;

ii) amino acids 122-139;

iii) amino acids 129-130; and

iv) amino acids 226-297;

in case the protein is human cytoplasmic dynein intermediate chain 2 (SEQ ID NO.: 65):

v) amino acids 155-165;

vi) amino acids 252-323;

vii) amino acids 148-165; and

viii) amino acids 1-149;

in case the protein is mouse DCTN 1 (SEQ ID NO.: 67):

i) amino acids 39-150;

ii) amino acids 1006-1021; and

iii) amino acids 133-899; or

in case the protein is human DCTN1 (SEQ ID NO.: 68):

iv) amino acids 39-150;

v) amino acids 1006-1021; and

vi) amino acids 133-899.

175. (Original) The method according to claim 174, wherein

a) if the protein is cytoplasmic dynein intermediate chain 1 (SEQ ID NOS.: 61 or 62), said amino acid is any one of the amino acids specified in Table 20;

b) if the protein is cytoplasmic dynein intermediate chain 2 (SEQ ID NOS.: 64 or 65), said amino acid is any one of the amino acids specified in Table 21;

c) if the protein is DCTN 1 (SEQ ID NOS.: 67 or 68), said amino acid is any one of the amino acids specified in Table 22.

176. (Original) An oligonucleotide suitable for identifying a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex.

177. (Previously Presented) An oligonucleotide according to claim 176, the nucleotide sequence of which corresponds to a nucleotide sequence within said allele, which contains a mutation that is indicative of an increased risk of a mammalian subject, particularly a human subject, of developing a neurodegenerative disease.

178. (Previously Presented) An oligonucleotide according to claim 176, which is suitable for hybridizing to the nucleic acid of said allele or a portion of its nucleic acid under stringent conditions.

179. (Previously Presented) An oligonucleotide according to claim 176, which is suitable as primer for amplifying the nucleic acid of said allele or a portion of its nucleic acid.

180. (Previously Presented) A kit for identifying a predisposition of a mammalian subject, particularly a human subject, for developing a neurodegenerative disease, or for identifying an association of a neurodegenerative disease of said subject with a mutation in an allele coding for a protein, which is a subunit of the dynactin/dynein complex, said kit comprising one or more oligonucleotides according to claim 176.

181. (Previously Presented) A kit for identifying a predisposition of a mammalian subject, particularly a human subject, for developing a neurodegenerative disease, or for identifying an association of a neurodegenerative disease of said subject with a mutation in an allele coding for a protein, which is a subunit of the dynactin/dynein complex, said kit comprising at least two oligonucleotides according to claim 179.

182. (Previously Presented) The kit according to claim 180, further comprising instructions to use the oligonucleotide or the oligonucleotides for identifying said predisposition in said subject or said association of the neurodegenerative disease of said subject with said mutation.

183. (Previously Presented) A solid support, wherein at least two oligonucleotides according to claim 175 are individually fixed to separate areas of the solid support to form an array, wherein said solid support is a glass chip, preferably a glass chip with a modified surface.

184 – 185. (Canceled)

186. (Previously Presented) A composition comprising:

(a) the cytoplasmic dynein heavy chain1 polypeptide of claim 11; and

(b) a pharmaceutically acceptable carrier.

187. (Previously Presented) A composition comprising:

(a) the cytoplasmic dynein heavy chain1 polypeptide of claim 27; and

(b) a pharmaceutically acceptable carrier.

188. (Previously Presented) A composition comprising:

(a) the cytoplasmic dynein heavy chain1 polypeptide of claim 37; and

(b) a pharmaceutically acceptable carrier.

189. (Previously Presented) A composition comprising:

(a) the murine cytoplasmic dynein heavy chain1 polypeptide of claim 38; and

(b) a pharmaceutically acceptable carrier.

190. (Previously Presented) A composition comprising:

(a) the human cytoplasmic dynein heavy chain1 polypeptide of claim 39; and

(b) a pharmaceutically acceptable carrier.

191. (Previously Presented) A polynucleotide, preferably isolated, comprising a nucleic acid sequence encoding a cytoplasmic dynein heavy chain1 polypeptide of claim 11.

192. (Previously Presented) A polynucleotide, preferably isolated, comprising a nucleic acid sequence encoding a cytoplasmic dynein heavy chain1 polypeptide of claim 27.

193. (Previously Presented) A polynucleotide, preferably isolated, comprising a nucleic acid sequence encoding a cytoplasmic dynein heavy chain1 polypeptide of claim 37.

194. (Previously Presented) A polynucleotide, preferably isolated, comprising a nucleic acid sequence encoding a cytoplasmic dynein heavy chain1 polypeptide of claim 38.

195. (Previously Presented) A polynucleotide, preferably isolated, comprising a nucleic acid sequence encoding a cytoplasmic dynein heavy chain1 polypeptide of claim 39.

196 – 208. (Canceled)

209. (Previously Presented) A method for the prevention, treatment or amelioration of a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject,

particularly a human subject, comprising the step of administering to the subject a cytoplasmic dynein heavy chain1 polypeptide of claim 11.

210. (Previously Presented) A method for the prevention, treatment or amelioration of a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject, particularly a human subject, comprising the step of administering to the subject a cytoplasmic dynein heavy chain1 polypeptide of claim 27.

211. (Previously Presented) A method for the prevention, treatment or amelioration of a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject, particularly a human subject, comprising the step of administering to the subject a cytoplasmic dynein heavy chain1 polypeptide of claim 37.

212. (Previously Presented) A method for the prevention, treatment or amelioration of a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject, particularly a human subject, comprising the step of administering to the subject a cytoplasmic dynein heavy chain1 polypeptide of claim 38.

213. (Previously Presented) A method for the prevention, treatment or amelioration of a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject, particularly a human subject, comprising the step of administering to the subject a cytoplasmic dynein heavy chain1 polypeptide of claim 39.

214. (Previously Presented) The method of claim 86, wherein the method comprises the additional step of determining that the cytoplasmic dynein heavy chain1 encoded by said polynucleotide is a modified cytoplasmic dynein heavy chain1 polypeptide, wherein:

(a) the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of at least one amino acid residue in the wild type cytoplasmic dynein heavy chain1 sequence;

(b) the position of said amino acid residue in the cytoplasmic dynein heavy chain1 sequence is selected from those positions at which, in each of the wild type cytoplasmic dynein heavy chain1 reference sequences, the identity of the wild type amino acid residue is conserved; and

(c) said wild type cytoplasmic dynein heavy chain1 reference sequences consist of:

(i) SEQ ID NO:18 (*Homo sapiens*);

(ii) Genbank Accession No. NP_062099 (*Rattus norvegicus*); and

(iii) Genbank Accession No. NP_084514 (*Mus musculus*).

215. (Previously Presented) The method of claim 86, wherein the method comprises the additional step of determining that the cytoplasmic dynein heavy chain1 encoded by said polynucleotide is a modified cytoplasmic dynein heavy chain1 polypeptide, wherein the modification is an amino acid substitution in the wild type cytoplasmic dynein heavy chain1 sequence at a position selected from the group consisting of:

(a) a position corresponding to position 1055 of the amino acid sequence as shown in SEQ ID NO:2; and

(b) a position corresponding to position 1057 of the amino acid sequence as shown in SEQ ID NO:19.

216. (Previously Presented) The method of claim 86, wherein the method comprises the additional step of determining that the cytoplasmic dynein heavy chain1 encoded by said polynucleotide is a modified cytoplasmic dynein heavy chain1 polypeptide, wherein:

(a) the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of at least one amino acid in the wild type cytoplasmic dynein heavy chain1 sequence;

(b) a biological activity of said modified cytoplasmic dynein heavy chain1 polypeptide is altered by at least 10% in comparison to the activity of the wild type cytoplasmic dynein heavy chain1 polypeptide.

217. (Previously Presented) The kit according to claim 181, further comprising instructions to use the oligonucleotide or the oligonucleotides for identifying said predisposition in said subject or said association of the neurodegenerative disease of said subject with said mutation.